

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

PHENOTHRIN

(Most or all studies were performed with D-phenothrin = Sumithrin)

Chemical Code # 002093, Tolerance # 50175
SB 950 # 232

November 23, 1987

Revised 10/19/89, 2/14/92, 12/22/92, 6/20/96

I. DATA GAP STATUS

Chronic toxicity, rat:	No data gap, possible adverse effect
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, rat:	No data gap, possible adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect
Reproduction, rat:	No data gap, possible adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time. An inadequate study, with no adverse effect indicated, is on file.

Toxicology one-liners are attached.

In the 1-liners below:

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

Revised by Aldous, 2/14/92, 12/22/92, 6/20/96.

File name: T960620

Note: these pages contain summaries only. Individual worksheets may identify additional effects.

Record numbers through 143777 (Document 50175-067) listed by the Pesticide Registration Library have been rectified with those listed in the Toxicology Summary. Some record numbers over 900000 are included.

The registered product in California is phenothrin. Most submitted studies (and all studies classified as **acceptable** as of 6/20/96) employ d-phenothrin under the trade name Sumithrin®. See Farm Chemicals Handbook or specific studies which cross-reference names of the active ingredient (as Document No. 50175-040, Record No. 074698). Aldous, 6/20/96.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

COMBINED, RAT

****50175-069 143777** Aughton, P., "Sumithrin: Combined oncogenicity and toxicity study by dietary administration to F-344 rats for 104 weeks", Huntingdon Life Sciences Limited, Dec. 11, 1995. Lab Report No. 94/0987. Rats were dosed at 0, 1000, 10000, or 20000 ppm Sumithrin (94% purity). There were 50/sex/group allocated for the oncogenicity study, 10/sex/group for the 1-yr interim sacrifice group, and an additional 20/sex/group for in-life toxicology studies (especially hematology and clinical chemistry). NOEL = 1000 ppm, based mainly on reduced body weights, "thin" appearance and hunched posture (females only), increased liver weights, liver histopathology (particularly panacinar hepatocytic hypertrophy), elevations in circulating enzymes generally interpreted to be indicators of liver pathology (alkaline phosphatase, gamma-glutamyl transpeptidase, and leucine aminopeptidase), and minor hematology changes (decreased HCT, Hb, and fibrinogen levels). Hepatocellular tumors, particularly carcinomas, were elevated at high doses in both sexes: incidences of carcinomas in controls through increasing dose groups were 0, 0, 2, and 5 for males and 0, 0, 1, and 8 for females. Liver pathology, including tumors, is a "**possible adverse effect**". There are indications that higher dose levels may have exceeded MTD criteria: (1) 20000 ppm female body weights were about 20% lower than controls by mid-study, and 27% by study termination. (2) Mortality of 10000 ppm and 20000 ppm males and of 20000 ppm females was substantially **lower** than corresponding controls, suggesting that the normal aging processes were upset. (3) A major factor in this differential mortality was a **reduction** in the degree of chronic progressive nephropathy in higher dose groups: this was probably related to subsequent reduction of mineralization of certain tissues, such as aorta and glandular stomach at 10000 to 20000 ppm in both sexes, as well as a sharp reduction in parathyroid hyperplasia in 20000 ppm males and females. These changes are entirely consistent with "end stage" nephropathy in F-344 rats. These indications that dose levels at or above 10000 ppm exceeded "tolerated" dose levels, in addition to the strong dose-response of panacinar hepatocytic hypertrophy at 10000 ppm and above (plausibly indicative of pre-neoplastic changes in highly perturbed livers), should be considered in interpretation of tumor data. Study is **acceptable**. Kishiyama and Aldous, 6/7/96.

50175-063 127937, 127938, and 127939 Interim results for Record # 143777, only a few pages each; all examined by J. Gee on 1/26/94 without worksheet.

50175-060 121984 "Sumithrin: Toxicity Study by the Dietary Administration to F-344 Rats for 13 Weeks", (P. Aughton, Life Science Research Limited, LSR Report 91/0942, 3/13/92). Sumithrin technical, purity 93.8%, was fed in diet at 0, 300, 1000, 10000 or 20000 ppm to ten F-344 rats/sex/group for 13 weeks. This study was used to set dose levels for the combined study, 50175-069 143777, above. This study identified many of the effects seen in the primary study, including hepatocytic hypertrophy (limited to the centriacinar area in 20000 ppm males and females in the 13-week study). Parameters with responses similar to those of the combined study included decreased body weight gain, liver weight increases, minor RBC parameter changes, increased plasma albumin and plasma alkaline phosphatase, decreased plasma glucose, and urinalysis findings of elevated specific gravity and decreasing pH. The range of dose levels selected for the primary study was defensible, considering the findings of this 13-wk study. No DPR worksheet is required at this time, since this is not a required study type, and the findings are very similar to the combined study. One-liner is by Kishiyama and Aldous, 6/10/96.

NOTE: DPR received a courtesy copy of this FIFRA 6(a)(2) notice, dated 12/14/94, regarding the liver tumors in Record No. 143777, above. This letter has no record nor document number. The cover letter from A.L. Lawyer, representing Sumitomo, was dated Jan. 12, 1995. Aldous, 6/20/96.

50175-066 130821 Status report of combined study (Record No. 143777, above), including protocol amendments. No review necessary, Aldous, 6/20/96.

50175-059 121978 and 121979 Protocol and amendments for Record No. 143777, above (no worksheet). Aldous, 6/20/96.

50175-033 073209 Martin, P.A., "Sumithrin: Combined toxicity and oncogenicity study in rats (ET-71-0102)". (Life Science Research, Project ID 85/SUM003/586, 1-87). Sumithrin, batch 10102, 92.6%, was administered to Fischer 344 rats in the diet at 0, 300, 1000, or 3000 ppm. Fifty/sex/group were assigned to a lifetime study: terminal sacrifices (based on survival) were 105 wk (males) or 118 wk (females). Additional treated groups of 30/sex were assigned to a "chronic" study: these were used for blood samples and an interim sacrifice at 52 weeks of 10/sex. Only the lifetime study animals plus the 10/sex assigned to interim sacrifice from the chronic study were examined microscopically. NOEL = 1000 ppm (small decrease in female body weights; small increase in female relative liver weights; increased incidence, in males only, of periacinar hepatocytic hypertrophy, and of dilatation of sinuses of the mesenteric lymph nodes). No adverse effects indicated. UNACCEPTABLE: Dose range is not justified. Shimer and Aldous, 2/14/92.

NOTE: A Rebuttal Response dated 12/16/92 by C. Aldous classified this study as "upgradeable".

50175-039 074277 Yappup, V.M., et al., "Sumithrin: Toxicity in Dietary Administration to Rats Over 13 Weeks", (Life Science Research, 2/83). This was the range-finding study for 50175-033 073209, above (discussed in Background section of DPR review of 2/14/92).

50175-057 Records 116020 to 116029 Several short records submitted to justify dosage levels employed in study 50175-033 073209, above (see rebuttal response of Aldous, 12/16/92).

50175-057 116030 Summary of 50175-060 121984, above.

CHRONIC TOXICITY, RAT

023 052524 "Two-Year Chronic Toxicity Study of S2539 in Rats", IBT, 2/19/80. S2539 was incorporated in the diets of Charles River rats at 0, 200, 600, 2000 or 6000 ppm for 24 months, 50/sex/group. NOEL = 2000 ppm, decreased body weight for males, increased liver weight for females, decreased food consumption, increased SGPT for males at 24 months. Report states no adverse effects, however this cannot be independently assessed from this study. UNACCEPTABLE. Not upgradeable. **Invalid IBT study.** Shimer and Silva, 10/15/87.

EPA one-liner: Supplementary, Systemic NOEL = 2000 ppm (body weight and organ weight changes). No conclusions for oncogenic aspects.

CHRONIC TOXICITY, DOG

****50175-036 073212** Cox, R.H., "Chronic Toxicity Study in Dogs with Sumithrin, T.G." (Hazleton Laboratories America, Inc., Study No. 343-173, April 2, 1987). Technical grade Sumithrin, Lot No. 41101, 92.7%, was given to beagle dogs in the diet at 0, 100, 300, 1000 or 3000 ppm (dose adjusted for purity), 4/sex/group, for 52 weeks. NOEL of 300 ppm was based on focal degeneration of the adrenal cortex (with associated mononuclear infiltration), and on diffuse hepatocellular enlargement

(both in males at 1000 ppm and above). These changes were seen in some females at 3000 ppm. No adverse effect. ACCEPTABLE. Shimer and Aldous, 1/22/92.

50175-024 052525 "Subchronic Toxicity Study in Dogs S2539-F Final Report", (Hazleton Laboratories, 9/9/81). Sumithrin Technical, lot 91137, 95.5% and lot 00218, 93.1%, was fed to beagles in the diet at 0, 100, 300 or 1000 ppm for 26 weeks, 6/sex/group. No adverse effects, NOEL = 300 ppm, slight elevation of serum alkaline phosphatase and absolute/relative liver weight in high dose males and females with equivalent trend in intermediate dose males. No microscopic or clinical changes observed. UNACCEPTABLE. Not upgradeable. MTD not reached, no dose justification. Not a 1 year study. Shimer and M. Silva, 10/15/87.

EPA one-liner: Guideline (Subchronic). NOEL = 300 ppm (liver weight and alkaline phosphatase increases).

ONCOGENICITY, RAT

See Combined, Rat, above.

ONCOGENICITY, MOUSE

****50175-034 073210** Amyes, S.J., "Sumithrin: Oncogenicity and Toxicity Study in Mice (ET-71-0109)". Life Science Research, Project ID 86/SUM007/166, dated April, 1987. Sumithrin, Lot no. 21005, 92.9%, was fed to B6C3F1 mice in the diet at 0, 300, 1000 or 3000 ppm for 104 weeks. Fifty/sex/group were designated for the entire two-year exposure. An additional 40/sex/group were sacrificed at interim periods: 10/sex/group at 26 and 53 weeks, with the remainder sacrificed at 78 weeks. Only the 53 week interim sacrifice animals and the mice assigned to the lifetime study were examined histologically. NOEL for males = 300 ppm [minor dose-related increases in liver weights, and (at mid-study only) incidence of "periacinar hepatocytic hypertrophy with increased eosinophilia" at 1000 ppm and above]. The same histological changes were noted in a few 3000 ppm females. Also, 3000 ppm (and to a minimal extent, 1000 ppm) females had small liver weight increases. There were slight body weight decreases at 3000 ppm in both sexes (statistically significant only in males). There was an equivocal increase in hepatocellular tumors in 3000 ppm females, primarily indicated by an increase in carcinomas. This is a **"possible adverse effect"**. Study is **acceptable as an oncogenicity study only**. Shimer and Aldous, 2/14/92.

50175-039 074276 Ames, S.J., et al., "Sumithrin: Five Week Range-Finding Toxicity Study in Mice", (Life Science Research, Ltd., 6/83). (Data were considered in review of lifetime study, Record No. 073210, above).

REPRODUCTION, RAT

****50175-067 135734** Hoberman, A.M., "Reproductive effects of Sumithrin* administered orally via the diet to CrI:CD* VAF/Plus* rats for two generations", Argus Research Laboratories, Inc., 2/23/95. Sumithrin*, 94% purity, was given in diet at 0, 1000, 3000, and 10000 ppm (no adjustment for purity) to 30 rats/sex/group for 2 generations (1 litter/generation). Parental NOEL = 1000 ppm (reduced body weight gain, slightly reduced food consumption, increased liver weights and hepatocellular hypertrophy (both in females), and focal bile duct proliferation (males). Mating and fertility NOEL = 10000 ppm (no effects). Fetal/pup viability and growth NOAEL = 1000 ppm (reduced pup weight at birth, and dose-related reduction in pup weight gain through weaning and beyond). Pup weights in 1000 ppm F2 pups were also significantly reduced ($p < 0.05$) through day 14 postpartum, however the degree of difference was slight. There was no significant body weight difference by day 21. Thus this "effect level" is not considered to be "adverse". Incidences and/or severities of all the above parental rat findings were manifest in both sexes at 10000 ppm. Organs weights of pituitary glands,

uteri, and ovaries were reduced in 10000 ppm females of both generations. The ovaries of F0 and F1 females had fewer corpora lutea than controls. All of these changes should be considered as "**possible adverse effects**". The doses associated with these findings were very large; sufficient to cause large body weight reductions and liver histopathology. The rather high NOAEL of 1000 ppm should be considered in interpreting these results. Study is **acceptable**. Kishiyama and Aldous, 6/18/96.

50175-064 127923 An "Adverse Effects Disclosure" for Record No. 135734, above, dated 12/28/93. No "review" of disclosure is needed. Aldous, 6/20/96.

50175-059 121980 Protocol for the range-finding study for Record No. 135734, above, dated 4/21/92. No "review" is needed. Aldous, 6/20/96.

50175-059 121981 Protocol for Record No. 135734, above, dated Nov. 9, 1992. No "review" is needed. Aldous, 6/20/96.

50175-063 127936 Interim results for Record No. 135734, only 2 pages, examined by J. Gee on 1/26/94 without worksheet.

50175-035 073211 Tesh, J.M., Willoughby, C.R., and Fowler, J.S.L., "Sumithrin: Effects Upon Reproductive Performance of Rats Treated Continuously Throughout Two Successive Generations (ET-61-0101)". (Life Science Research, Project ID 85/SUM009/331, 11-86). Sumithrin, d-phenothrin, lot No. 21005, 92.9%, was fed to CD rats in the diet at 0, 300, 1000 or 3000 ppm continuously for a two generation reproduction study, 2 litters each generation, 30/sex/group. The F1B litters were used for F1 adults. NOAEL > 3000 ppm: trivial decreases in body weights at some time intervals, and small increases in liver weights in males or females (statistically significant increase in absolute liver weights of 3000 F0 females only). No reproductive or developmental effects. NOEL = 1000 ppm. No adverse effects. UNACCEPTABLE. Dose level appears not justified. Study can be upgraded if and only if it can be demonstrated that appreciably higher dosages could not have been tolerated. The report of the preliminary reproduction study which forms the basis for dose selection for this study is requested. Shimer and Aldous, 2/14/92.

50175-060 121983 Tesh, J.M., C.R. Willoughby and R.C. Secker, A range-finding study: "Sumithrin: Effects of Dietary Administration upon Reproductive Performance in the Rat", Life Science Research Limited, LSR Report No. 83/SUM008/116, 9/9/83. Sumithrin (d-Phenothrin, 92.6% purity), was fed in diet at 0, 1000, 3000 or 10000 ppm to 6 Sprague-Dawley rats/sex/group. Treatment was 15 days prior to mating, and continuously through gestation and for 4 days post partum. High dose females had a transitory body weight loss during the first few days of treatment, then gained in parallel to other groups. These dams had slightly fewer implantation sites and fewer live born pups than other groups (12.7 live pups on day 1 in 10000 ppm group, vs. 14.8 in controls). Pup growth was unaffected. There is no information in this pilot study which requires special consideration in hazard assessment, nor is a worksheet necessary, given that the primary study has been reviewed. These data were submitted in response to a request by DPR for substantiation that dose levels in the primary LSR study of 1986 (Record No. 073211) were justifiable. The submission of the acceptable Argus study above makes further consideration of the LSR study a moot issue. Kishiyama and Aldous, 6/19/96.

TERATOLOGY, RAT

** 040 074698 Tesh, J.M., Willoughby, C.R., Lambert, E.P., Wilby, O.K., and Tesh, S.A., "Sumithrin: Effects of Oral Administration Upon Pregnancy in the Rat" (Life Science Research, England, LSR Report No: 83/SUM005/084, 5/6/83). d-Phenothrin, batch 10102, 92.6%, was administered to groups of 20 pregnant CD rats by oral gavage on days 6 through 15 of gestation at 0 (corn oil

vehicle), 300, 1000, or 3000 mg/kg/day. Decreased maternal weight gain and food consumption, and developmental delay evidenced by small and immature fetuses was observed at a dose of 3000 mg/kg/day. These are not considered to pose a possible adverse health effect since they occur at a dose level above the limit test of 1000 mg/kg/day. Maternal NOEL = 1000 mg/kg/day (decreased maternal weight gain and food intake at 3000 mg/kg); Developmental NOEL = 1000 mg/kg/day (decreased fetal weight and signs of developmental delay at 3000 mg/kg). ACCEPTABLE study. Chernoff, 10/10/89.

022 052504 Incomplete version of record no. 074698 reviewed by M. Silva, 10/14/87.

TERATOLOGY, RABBIT

002 025359 Rutter, H.A., "Teratology Study in Rabbits, S-2539 Forte (Phenothrin), Final Report", (Hazleton Labs, 2/18/74). S-2539, no description given, was administered to pregnant New Zealand White rabbits by gavage on days 6 to 18 of gestation at 0 (corn oil), 10, 100, or 1000 mg/kg/day, 9 to 13/group. No adverse effect. Maternal NOEL = 1000 mg/kg/day (HDT), Developmental NOEL = 1000 mg/kg/day (HDT). No toxicity noted at any level. 1000 mg/kg/day acceptable by limit test. UNACCEPTABLE. No description of test substance, no individual data. Christopher, 6/12/85.

EPA one liner: No core grade. Teratogenic NOEL > 1000 mg/kg, Fetotoxic NOEL = 100 mg/kg (depressed viable fetuses).

50175-008 970962 duplicate of 002 025359, above.

**50175-045 075878 Nemec, M.D., "A Teratology Study in Rabbits with Sumithrin" (WIL Research Laboratories Inc., Project No. WIL-118003, 5/11/89). Sumithrin technical, Lot No. 61001, 94.1%, was given to artificially inseminated New Zealand White rabbits by gavage at nominal dose levels of 0 (0.5% carboxymethyl cellulose), 30, 100, 300 or 500 mg/kg/day, 20/group, days 7-19 of gestation. Maternal toxicity NOEL = 100 mg/kg/day (small decrements in body weight gain and in food consumption during treatment, also slight increases of hair loss in inguinal area at 300 mg/kg/day). At 500 mg/kg/day, above changes were more marked, and there were also decreases in the extent of defecation and urination, as well as an apparent treatment-related increase in abortion frequency. Developmental NOEL = 300 mg/kg/day (hydrocephaly, usually accompanied by domed head). No adverse effects. ACCEPTABLE. Shimer and Aldous, 2/14/92.

50175-044 075877 "Range-Finding Teratology Study in Rabbits With Sumithrin" [cited in DPR review for Rec. #075878, above].

TERATOLOGY, MOUSE

008 970961 Nakamoto, N., *et al.*, "S-2539 Forte (Phenothrin) Teratology Study in Mice", (Sumitomo Chemical Co. Ltd., 8/73). S-2539, no description, was administered to ICR-SLC mice on days 7 to 12 of gestation at 0 (aqueous Tween 80), 30, 300 or 3000 mg/kg/day. UNACCEPTABLE. No justification of dose, route of administration not stated, dosing solutions not analyzed, species not justified, missing individual data. Christopher, 6/13/85.

EPA one-liner: Supplementary. Teratogenic NOEL > 3000 mg/kg (HDT), Fetotoxic NOEL = 30 mg/kg (accelerated skeletal ossification).

50175-002 970963 Duplicate of 008 970961, above.

GENE MUTATION

002 030543 "Mutagenicity of Some Synthetic Pyrethroids Bacterial Test Systems: Reversion Test

(Ames Method) - *E. coli* and *S. typhimurium* Host Mediated Assay - ICR Male Mice and *S. typhimurium* G46 as the Host and the Indicator Respectively", (Sumitomo Chem. Co., 8/79). *E. coli* and *S. typhimurium* were used to assay phenothrin for gene mutation. No adverse effects, however the study was UNACCEPTABLE and not upgradeable. Inadequate protocol, no metabolic activation, too few levels tested, too few strains of bacteria tested, inadequate discussion of methods. No way of affirming that the test substance reached the target *in vivo*. Christopher, 6/12/85.

** 50175-022 052508 Kishida, F. and Suzuki, H., "Gene Mutation test of Sumithrin in Bacterial System", (Sumitomo Chem, Co., 11/7/81). Sumithrin, lot 10113, 93.5%; *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *E. coli* WP-2 uvrA were used in gene mutation assays, with and without metabolic activation at 0, 10, 50, 100, 500, 1000 and 5000 ug/plate. Duplicate plates, repeat trial. No increase in revertants reported. ACCEPTABLE. Shimer and Silva, 10/15/87.

EPA one-liner: Acceptable. Not mutagenic up to and including 500 ug/plate with and without metabolic activation.

CHROMOSOME EFFECTS

50175-022 052509 Suzuki, H., and Hara, M., "*In vivo* Chromosomal Aberration Test of Sumithrin on Bone Marrow Cells of Mice", (Sumitomo Chem. Co., 12/14/81). Sumithrin, lot 10113, 93.5% was given to male mice intraperitoneally at single doses of 2,500, 5,000 or 10,000 mg/kg. Mice were sacrificed 6, 24, or 48 hours post-treatment, 6/group, 12 untreated controls. Counted 50 metaphase cells per animal, defined types of aberrations. No dose response increase in aberrations was observed. UNACCEPTABLE. upgradeable. Female mice were not used, historical controls should be included. Shimer and Silva, 10/15/87.

EPA one-liner: No conclusion. Not mutagenic up to and including 10 gm/kg.

**50175-022 052510 Yoshitake, A., et al., "*In vitro* Chromosomal Aberration Test of S-2539F in Chinese Hamster Ovary Cells (CHO-K1)", (Sumitomo Chem. Co., 4/23/86). S-2539F (defined in Record No. 052504 as Sumithrin*), lot 50208, 92.6%, was examined in the *in vitro* chromosomal aberration test using Chinese hamster ovary cells in culture with and without S9 activation. In the absence of S9, the cells were treated at dose levels from 2×10^{-5} to 2×10^{-4} M for 24 and 48 hr. With S9, the dose levels were from 5×10^{-5} to 5×10^{-4} M for 6 hours. No increase in aberrations was reported. No justification for single harvest time for +S9 and first harvest at 24 hours for -S9. ACCEPTABLE. Shimer and Silva, 10/15/87.

DNA DAMAGE

002 030282 "Mutagenicity of Some Synthetic Pyrethroids Bacterial Test Systems - Repair Test to detect DNA Damaging Capacity of Allethrin, Phenothrin, Furamethrin, Permethrin and Resmethrin Using *E. coli*, *Bacillus subtilis* and *Salmonella typhimurium*", (Sumitomo Chemical Co. Ltd., 8/2/79). *E. coli*, *B. subtilis* and *S. typhimurium* were used to detect DNA damaging capacity of pyrethroids. UNACCEPTABLE. Inadequate protocol and report, no metabolic activation, inadequate description of test substance, inadequate methods section, single plates, too few levels, no retest. Christopher, 6/12/85.

**50175-022 052511 Forster, R., et al., "Unscheduled DNA Synthesis in Human Cells. Cell line: HeLa S3, Test Substance: Sumithrin", (Roma Toxicology Centre, 4/84). Sumithrin, lot 10202, 92.6%, was assayed for the induction of UDS in HeLa S3 cells. Test concentrations were 0.25, 0.5, 1, 2, and 4 mg/ml. Assayed with and without metabolic activation, 3 cultures per concentration, liquid scintillation counting. No induction of unscheduled DNA synthesis was reported. ACCEPTABLE. Guidelines call for 6 cultures per concentration, however there are sufficient data, due to use of 5 concentrations in triplicate. Shimer and Silva, 10/15/87.

50175-022 052523 Kishida, F., and Suzuki, H., "Studies on DNA-Damaging Capacity of Sumithrin with *Bacillus subtilis*", (Sumitomo Chem. Co., 11/7/81). Sumithrin, lot 10113, 93.5% was assayed with spores of *Bacillus subtilis* M45 and H17. The test compound was applied to a paper disk at the center of a spore containing agar plate. Dose levels were 10, 50, 100, 500, 1000 or 5000 ug/disk. Sumithrin caused no growth inhibition. Study done in triplicate, repeat trial. UNACCEPTABLE. Not upgradeable. No metabolic activation was used. No cytotoxicity was observed at the high dose therefore the study was a no test. Shimer and Silva, 10/15/87. EPA one-liner: No conclusion. Not mutagenic up to and including 5000 ug/disk.

NEUROTOXICITY

002 970960 "Neurotoxicity Study of D-Phenothrin (S-2539-Forte) in Rats by Repeat Oral Administration", (Sumitomo Chemical Co., 5/8/78). D-phenothrin, no description, was administered by gavage to Sprague Dawley rats for 5 days at 5000 mg/kg/day, 5/sex, then observed for 3 days. Not a guideline type study. UNACCEPTABLE. No justification is presented for species, dose level, dose regime, tissues taken length of observation period, etc. No positive control, test article not described. Christopher, 6/12/85.

Delayed neurotoxicity testing is not required for this class of compound at the present time.